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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,702	12/29/2005	Susanne Olausson	10400-000203/US	8760

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EXAMINER	
WANG, CHANG YU	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
12/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,702	OLAUSSON ET AL.	
	Examiner	Art Unit	
	CHANG-YU WANG	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57-61,71-83,93-101,103 and 113-118* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57-61, 71-83, 93-101,103 and 113-118* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/2/09 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed 11/2/09 is acknowledged. Claims 1-56, 62-70, 84-92, 102 and 104-112 are cancelled. Claims 57-58, 60, 71, 77, 81-83, 93, 100, and 101 are amended. Claims 113-118 are newly added. Claims 57-61, 71-83, 93-101,103 and newly added claims 113-118 are pending in this application and under examination in this office action.

3. Any objection or rejection of record, which is not expressly repeated in this office action, has been overcome by Applicant's response.

4. Applicant's arguments filed on 11/2/09 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Maintained

In view of the amendment filed on 11/2/09, the following rejections are maintained.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 57-61, 71-83, 93-101,103 and 113-118 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6548569 (Williams et al., issued on Apr 15, 2003, priority date Mar 25, 1999) in view of US Patent No. 5656605 (Hansson et al., issued Aug 12, 1997) and US. Patent No. 5584885 (Seckel, issued on Dec 17, 1996). The rejection is maintained for the reasons made of record.

Claims 57-61, 71-83, 93-101,103 and 113-118 as amended are drawn to a device/kit/biodegradable sheet for promoting regeneration of an injured nerve, comprising: a nerve encasement structure/biodegradable sheet/an dehydrate hydrogel and a plurality of biodegradable guiding fibers. The guiding fibers disclosed in the claimed device/kit/biodegradable sheet comprise polyhydroxybutyrate (PHB) and the PHB average molecular weight for the nerve encasement is within the range of 100,000-250,000daltons and the PHB average molecular weight for the guiding fiber is within the rang of 50,000 to $\leq$ 250,000 daltons wherein the guiding fibers have an in vivo degradation time (t1) that is less than tc, which is the required for establishing regenerated contact between ends of an injured nerve using the device for regeneration and wherein t1< 14+L/v and L/v $\leq$tc$\leq$14+L/v and wherein "L" is the nerve gap (mm) of the injured nerve and "v" is the axon growth rate (mm/day) of the injured nerve, typically 0.5-2mm/day. The nerve encasement structure has an in vivo degradation time (t2) that is longer than t1. The t2 is also longer than tr, which is the time required for the entire nerve regeneration process to be completed, and wherein t2>t1; t2>2 (L/v); and 2(L/v) $\leq$ tr $\leq$14+2(L/v).

Dependent claims are directed to as follows: the nerve encasement structure comprises a compressed non-woven sheet with an unidirectional fiber orientation (claims 71, 93) and the guiding units comprise a non-bonded fiber web with an unidirectional fiber orientation (claims 72, 94). Furthermore, the device/kit/sheet further comprises a dehydrate hydrogel matrix (claims 73, 95-96), an active substance or cell (claims 74-77, 97-99 and 103). Moreover, the guiding units occupy $\leq$2.0% by volume of the lumen formed by the nerve encasement structure (claim 77), the cross-section dimension of the guiding units is $\leq$50μm (claim 78), $\leq$20μm (claim 79), 5-15μm (claim 80). The device/kit/sheet is porous (claims 113-117).

On p. 14-15 of the response, Applicant argues that tc and tr represent time periods related to the nerve regeneration process and tc and tr are properties of the nerve to be regenerated and t1 and t2 define the in vivo degradation times of the biodegradable nerve encasement structure or the biodegradable guiding fibers and the t1 is always less than t2. Applicant argues that the structures and compositions of the nerve guides of Williams are not the same as those recited in independent claims 57, 60, 81, 83, 100 and 101 because Williams fails to indicate the molecular weight of the different structures of the nerve guide should invariably be selected from different parts of that range be composed of materials presenting different in vivo degradation times. Applicant argues that although Hansson teaches guide thread filament materials may consist of materials similar or identical to the materials used for a guide, Hansson is not concerned with molecular weights or degradation time of these materials and the

examples in Hansson are non-biodegeradable materials. Applicant argues that Seckel does not teach the use of a plurality of guiding fibers in a device for the regeneration of an injured nerve as in independent claims 57, 60, 81, 83, 100 and 101, and there is no indication that matrix element 58b should present an in vivo degradation or be degraded at any particular point in time. Applicant argues that there is no suggestion in the cited references that a material of low molecular weight is for certain parts of a nerve conduit and thus no incentive to differentiate the molecular weights of the nerve encasement structure and the guiding fibers as in independent claims 57, 60, 81, 83, 100 and 101. Applicant's arguments have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In contrast to Applicant's arguments, the cited references do render the claimed device obvious because Williams teaches a biodegradable device comprising poly-4-hydroxybutyrate (PHB) (see col.7, lines 31-33, in particular) in a form of porous conduit such as having the shape of the nerve conduit products of NEUROTUBE™ as incorporated by the references including US Patent NOs. 5735863, 5584885 and 5026381. Williams also teaches that the degradation rate of the PHB polymer in the nerve guide or biodegradable device is manipulated through addition of components to

the polymeric composition, selection of the chemical composition of the polyhydroxyalkanoate polymer through selection of monomeric units, as chemical linkages, which are incorporated into the polymer, by alteration of the linkages, chemical backbone or pendant groups, molecular weight, processing conditions, or form of the composition, and wherein the polyhydroxyalkanoate polymer has an average molecular weight of between 10,000 and 10,000,000 Dalton; and wherein the form of the composition refers to the porousness and surface area of the composition (see col. 10, lines 6-col. 12, line 22; col. 33-35, examples 4-5; col. 37-39, examples 6-11; col. 39, lines 41-46, in particular). Thus, Williams does teach that changing the molecular weight of the guiding fibers and the nerve encasement structure can change the degradation rate of guiding fibers and the nerve encasement. In addition, Williams teaches a spinal fusion device fabricated from PHB to improve the degeneration disc diseases (see col. 20, line 50-col. 21, line 52; col. 35-36, tables 6-7, in particular).

Although Williams does not explicitly teach that the average molecular weight of PHB is within the range of 100,000 to 250,000 Daltons for the nerve encasement and does not teach that is within the range of 50,000 to <250,000 for the guiding fibers as in recited in independent claims 57, 60, 81, 83, 100 and 101, Williams teaches that PHB polymers have an average molecular weight of between 10,000 and 10,000,000 Dalton (see col. 39-40, claim 1; col. 10, lines 6-col. 12, line 22; col. 33-35, examples 4-5; col. 37-39, examples 6-11; col. 39, lines 41-46, in particular). Williams also teaches that the units of PHB polymers are 10-100,000 and preferably 100-30,000units and that the molecular weight of the PHB polymers for biodegradable devices is between 10,000-

10,000,000Dalton (see col. 5, lines 40-col. 6, line 10; col. 39, claim 1, in particular). Williams also teaches that the device comprising PHB polymers can be coated or fabricated to medical device to improve their compatibility, tailoring their degradation and controlled release profiles (see col. 27, lines 1-35, in particular). Thus, it is obvious to modify the molecular weight of PHB to alter and make the degradation rate of the guiding fibers is less than that of the never encasement structure in the biodegradable device (such as a Neurotube) as disclosed by Williams because Williams teaches the range of 10,000 and 10,000,000 Daltons for the PHB in the Neurotube and also teaches alteration of the molecular weight of PHB in the Neurotube or nerve guide can change the degradation rate of the Neurotube or the nerve guide.

Note that

In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie*case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990), See MPEP 2144.05-I

"a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)" See MPEP 2144.05-I

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105USPQ 233, 235 (CCPA 1955)" See MPEP 2144.05-II

In addition, Williams teaches sheets made from PHB and PGA (which is the same as PLGA) (see col. 38-39, examples 10-11, in particular) and also teaches patches including silicone membranes, polyurethane, fascia, lata, Gore-Tex etc, which meets the limitation of "a dehydrate hydrogel matrix" and PHB foams coating of a PGA

non-woven mesh (see col. 16, line 63- col.17, line 7; col. 25, line 50- col. 27, line 35; col. 39, example 11, in particular). Furthermore, Williams teaches formation of PHB microspheres with the size of 1-10μm(see col. 39, example 12, in particular), which meet the limitation of " the cross-section dimension of the guiding units is ≤50μm, ≤20μm or 5-15μm as recited in instant claims 78-80.

Note that the instant specification only describes a conduit made from a non-woven sheet of polyhyroxybutryate (PHB) having a molecular weight of 140,000, a sheet thickness of 0.25mm and a weight per unit area of 10mg/cm2 and filled with non-bonded PHB fibers with an average molecular weight of 80,000 and cross-sectional dimensions within the range of 5-15μm wherein the conduit is able to repair a 10mm gap of an injured sciatic nerve. Although Williams does not explicitly teaches specific ti, tc, t1 and t2, the nerve guides/devices/kits/sheets disclosed by Williams have similar structures and compositions to those described in the instant specification. Thus, the nerve guides/devices/kits/sheets disclosed by Williams would also have the similar properties of t1, t2, tc and tr as recited in instant claims, which render the claimed devices/kits/sheets obvious.

Furthermore, although Williams does not teach an active substance and cells as recited in instant claims 75-76 and 98-99, Seckel (US 5584885; i.e. one of the incorporated references in the reference of Williams) teaches nerve guides (i.e. nerve conduits) comprising Schwann cells, growth factors and drugs as recited in instant claim

75-76 and 98-99 (see col.7, lines18-col.8, lines 29; col. 16, lines 22-60, in particular). Hasson teaches nerve guides for promoting nerve regeneration comprising a guide tube, guiding filaments and a therapeutic composition enclosed by the guide tube wherein both the nerve guide and the nerve filaments are composed of a nerve-growth stimulating agent in a matrix-forming material (see abstract). Hasson also teaches that the nerve guide tube is made of biological inert polymer such as polyglycolic acid (PGLA) and therapeutic composition such as methylcellulose gel and a nerve-growth stimulating agents such as IGF-like, NGF, PDGF and Schwann cells (see col. 2, lines 41-col. 3, line 24; col.2, line 42-col.5, line 7, in particular). The inert polymeric material includes collagen complexes, polylactic acid, polyglycolic acid, polyetraethyelen, silastic, poly-n-aceylglucosamine or polymer into which growth factors can be incorporated directly for the nerve guide tubes. The nerve guide thread filaments can be the same as the nerve guide tube or other compatible substances for formation of a cable of axon regeneration and the materials for carrier matrices include collagen, methylcelluose gel, fibrin other blood derived proteins, extracellular matrix such as Matrigel, Biomatrix and nerve-growth stimulating agents include Insulin like growth factors, FGF, a/bFGF, TGF, PDGF, BDGF, CNTF etc. and the cells include Schwann cells, endothelial cells, fibroblasts (see col.3, lines 5-24; col. 3, line 52-col.5, line 7, in particular).

It would have been obvious to a skilled artisan at the time the instant invention was made to make a device/kit/sheet having a nerve encasement structure and guiding units wherein the molecular weight of guiding units is less than that of the encasement

to optimize different molecular weights of PHB for the nerve encasement and guiding units to tailor the in vivo degradation time and compatibility of the device for nerve regeneration purposes. The skilled artisan would have been motivated to do so with an expectation of success because Williams teaches that PHB polymers with different molecular weights would degrade differently and the PHB polymers with a molecular weight between 10,000-10,000,000Dalton are expected to work for repair or regeneration and Hansson and Seckel teach a device encompasses a guide tube, guiding filaments and a therapeutic composition enclosed by the guide tube.

Note that

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980); see also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992). See MPEP § 2144.06.

"The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945)". See MPEP § 2144.07.

"Obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so. In re Kahn, 441 F.3d 977, 986, 78 USPQ2d 1329, 1335 (Fed. Cir. 2006)" See MPEP § 2143. 01-I.

Taken together, given the examination guidelines for determining obviousness under 35 U.S.C. 103 in view of the Supreme Court decision in KSR International Co. V. Teleflex Inc. 82 USPQ2d 1385 (2007) and the Examination Guidelines set forth in the Federal Register (Vol. 72, No. 195, October 10, 2007) and incorporated recently into the MPEP (Revision 6, September 2007), the following rationales to support rejection under 35 U.S.C. 103(a) are noted:

A) Combining prior art elements according known methods to yield predictable results.

B) Simple substitution of one known element for another to obtain predictable results.

C) Use of known technique to improve similar products in the same way.

D) Applying known technique to a known product ready for improvement to yield predictable results.

E) "Obvious to try" --- choosing form a finite number of identified, predictable solutions, with a reasonable expectation of success.

F) Some teachings, suggestion, or motivation in the prior art that would lead to one of ordinary skill to modify the prior art reference to arrive at the claimed invention. In this case, it is obvious to make the claimed devices/kits/sheets by using the known technique to a known product ready for improvement disclosed by Williams and is obvious by combining the teachings of Williams, Hansson and Seckel to yield predictable products because Williams teaches that PHB polymers with different molecular weights would degrade differently and the PHB polymers with a molecular weight between 10,000-10,000,000Dalton are expected to work for repair or regeneration and Hansson and Seckel teach a device encompasses a guide tube, guiding filaments and a therapeutic composition enclosed by the guide tube.

Conclusion

6. NO CLAIM IS ALLOWED.

7. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chang-Yu Wang, Ph.D.
December 14, 2009, 2009

/Chang-Yu Wang/
Examiner, Art Unit 1649